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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 09/890,875 | 08/07/2001 | Hiromu Ohnogi | OHNOGI=1 | 9130 |

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| EXAMINER |
|---|
| HUI, SAN MING R |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1617 | |

DATE MAILED: 05/07/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. 09/890,875 | Applicant(s) OHNOGI ET AL. | |
|---|---|---|---|
| | Examiner San-ming Hui | Art Unit 1617 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *14 February 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *4-8* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

The cancellation of claims 1-3 filed February 14, 2002 is acknowledged.

The outstanding warning of claims 1-2 is withdrawn in view of the cancellation of the claims.

The outstanding rejections of claims 1-3 under 35 USC 112, first and second paragraphs and 102 are withdrawn in view of the cancellation of the claims.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-8 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the treatment of liver degeneration, severe hepatitis, cirrhosis, cholestasia, neuronal degeneration, Alzheimer's disease, senile dementia, osteoporosis, diabetes, anemia, insufficient intrauterine growth, renal insufficiency, and immunodeficiency, does not reasonably provide enablement for other diseases that requires the enhancement of growth factor production of interleukin-12 production. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In the instant case, the specification fails to provide information that would allow the skilled artisan to practice the instant invention without undue experimentation.

Attention is directed to *In re Wands*, 8 USPQ2d 1400 (CAFC 1988) at 1404 where the court set forth the eight factors to consider when assessing if a disclosure would have required undue experimentation. Citing *Ex parte Forman*, 230 USPQ 546 (BdApls 1986) at 547 the court recited eight factors:

1) the quantity of experimentation necessary,

2) the amount of direction or guidance provided,

3) the presence of absence of working examples,

4) the nature of the invention,

5) the state of the prior art,

6) the relative skill of those in the art

7) the predictability of the art, and

8) the breadth of the claims.

Applicant fails to set forth the criteria that defines neither a "disease that requires enhancement of growth factor production, nor that of interleukin-12 production". Additionally, Applicant fails to provide information allowing the skilled artisan to ascertain these compounds without undue experimentation. In the instant case, only a limited number of " disease that requires enhancement of growth factor production, nor that of interleukin-12 production " examples are set forth, thereby failing to provide sufficient working examples. It is noted that these examples are neither exhaustive, nor define the diseases being treated or prevented. The pharmaceutical art is unpredictable, requiring each embodiment to be individually assessed for physiological activity. The instant claims read on **all** "disease that requires enhancement of growth

factor production, nor that of interleukin-12 production", necessitating an exhaustive search for the embodiments suitable to practice the claimed invention. Applicants fail to provide information sufficient to practice the claimed invention, absent undue experimentation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 4-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The expression "disease that requires enhancement of growth factor production, nor that of interleukin-12 production" in claims 4-8 renders the claims indefinite as to the diseases encompassed by the claims. Furthermore, it is unclear what amount of the active claimed compounds is encompassed by the claims.

The moieties $W_1$, $W_2$, and $W_3$ recited in claims 4 and 6 render the claims indefinite. $W_1$, $W_2$, and $W_3$ are "residue in which a SH group is removed from a SH group-containing compound". Since it is not clear what compound(s) is(are) encompassed by the term "SH group containing compound", it is not clear what moieties are encompassed by $W_1$, $W_2$, and $W_3$ herein.

Claims 7 and 8 recite the limitation "the method according to claim 5" in line 1 respectively. There is insufficient antecedent basis for this limitation in the claim. In

order to expedite prosecution herein, claims 7 and 8 are treated as they are depending from claim 6 which is apparently intended by the applicant.

***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 4-5 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 13-22 of U.S. Patent No. 6,177,592 ('592). Although the conflicting claims are not identical, they are not patentably distinct from each other because '592 teaches the pharmaceutical composition containing the instant claimed compounds of Formula II. Although '592 does not teach the amount of the compounds to be included, it would have been obvious to one of ordinary skill in the art at the time the invention was made to optimize the dosage of the active compounds in the composition. One of ordinary skill in the art would have been motivated to optimize the dosage of the active because it is within the purview of the artisan, absent evidence to the contrary.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 4-8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Koyama et al. (WO98/39291, its English equivalent, EP 0 984 001 A1, is from the IDS received November 7, 2001) in view of Hogde-Dufour et al. (Proc. Natl... Acad. Sci. USA, 1998; 95: 13806-13811).

Koyama et al. teaches the compounds of Formula II herein which can inhibit Tumor necrosis factor (TNF) activities and production (See page 13, lines 7-18). Koyama et al. teaches the dosage of the compounds herein to be 0.1 $\mu$g – 100mg/kg/day (See page 13, line 23). Koyama et al. also teaches that the compounds can be administered orally and can be incorporated into food and/or beverage (See page 13, line 32-33).

Koyama et al. does not expressly teach that the compounds of Formula II herein are capable to enhance the production of interleukin-12.

Hogde-Dufour et al. teaches TNF as inhibiting the production of interleukin-12 by inhibiting interferon $\gamma$ production (See the abstract, also page 13808 col. 1). Hogde-Dufour et al. also teaches that neutralization of TNF can augment the production of interleukin-12. (See page 13808, col. 1, second paragraph).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to employ the compounds of Formula II herein, in the composition and method of enhancing the production of interleukin-12; thereby treating diseases treatable with the enhanced production of interleukin-12.

One of ordinary skill in the art would have been motivated to employ the compounds of Formula II, herein, in the composition and method of enhancing the production of interleukin-12 and thereby treating diseases treatable with the enhanced production of interleukin-12 because based on the Hogde-Dufour et al. teachings of neutralizing TNF to increase the production of interleukin-12. Therefore, employing any known compounds that inhibit TNF production and these activities, including the compounds of Formula (II) herein would have been reasonably expected to be useful and effective in the method and composition herein.

It is applicant's burden to demonstrate unexpected results over the prior art. See MPEP 716.02, also 716.02 (a) - (g). Furthermore, the unexpected results should be demonstrated with evidence that the differences in results are in fact unexpected and unobvious and of both statistical and practical significance. *Ex parte Gelles*, 22 USPQ2d 1318, 1319 (Bd. Pat. App. & Inter. 1992). Moreover, evidence as to any unexpected benefits must be "clear and convincing" *In re Lohr*, 137 USPQ 548 (CCPA 1963), and be of a scope reasonably commensurate with the scope of the subject matter claimed, *In re Linder*, 173 USPQ 356 (CCPA 1972). In the instant case, data of example 6 have been considered but are not found persuasive. The data in example 6 merely demonstrate the effectiveness of the compounds herein to enhance the production of

interleukin-12. This is seen to be an expected effect based on the cited prior art. No convincing and clear unexpected result is seen.

***Response to Arguments***

Applicant's arguments with respect to claims 4-8 have been considered but are moot in view of the new ground(s) of rejection.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to San-ming Hui whose telephone number is (703) 305-

1002. The examiner can normally be reached on Mon 9:00 to 1:00, Tu - Fri from 9:00 to 6:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Minna Moezie, J.D., can be reached on (703) 308-4612. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4556 for regular communications and (703) 308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1235.


San-ming Hui
May 6, 2002